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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Richard Axel et al.	
Serial No.	:	08/484,136	Examiner: M. Latimer
Filed	:	June 7, 1995	Group Art Unit: 1805
For	:	DNA CONSTRUCT FOR PRODUCING PROTEINACEOUS MATERIAL IN EUCARYOTIC CELLS	

1185 Avenue of the Americas
New York, New York 10036
November 26, 1997

Honorable Assistant Commissioner
for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. § 1.56, applicants would like to direct the Examiner's attention to the following references which are listed on Form PTO-1449 (Exhibit 1). References 1-23, 25, 27-48, 50-53, 56-59, 61, 63, 64, 66, 69-71, 73, 74, 77-93, 95, 97, 98, 101, 105-107, 109, 112, and 113 are attached hereto as Exhibits 2-90, respectively:

1. U.S. Patent No. 3,800,035 for Goore, M., "Production of Interferon from human leucocytes in the absence of serum" issued March 26, 1974 (filed Dec. 7, 1971)(Exhibit 2);

2. U.S. Patent No. 4,195,125 for Wacker, A., "Process for obtaining insulin producing animals cells" issued March 25, 1980 (filed Dec. 20, 1978)(Exhibit 3);

3. U.S. Patent No. 4,237,224 for Cohen, S.N. and Boyer, H.W., "Process for producing biologically functional molecular chimeras" issued Dec. 2, 1980 (filed Jan. 4, 1979)(Exhibit 4);

4. U.S. Patent No. 4,264,731 for Shine, J., "DNA joining method" issued Apr. 28, 1981 (filed Apr. 21, 1978)(Exhibit 5);

5. U.S. Patent No. 4,342,832 for Goeddel, D.V. et al., "Method of constructing a replicable cloning vehicle having quasi-synthetic genes" issued Aug. 3, 1982 (filed July 5, 1979) (Exhibit 6);

6. U.S. Patent No. 4,356,270 for Itakura, K., "Recombinant DNA cloning vehicle" issued Oct. 26, 1982 (filed Nov. 5, 1979)(Exhibit 7);

7. U.S. Patent No. 4,363,877 for Goodman, H.M. et al., "Recombinant transfer vectors" issued Dec. 14, 1982 (filed Apr. 19, 1978)(Exhibit 8);

8. U.S. Patent No. 4,366,246 for Riggs, A.D., "Method for microbial polypeptide expression" issued Dec. 28, 1982 (filed Nov. 5, 1979)(Exhibit 9);

9. U.S. Patent No. 4,399,216 for Axel, R. et al., "Processes for inserting DNA into eucaryotic cells and for producing proteinaceous materials" issued Aug. 16, 1983 (filed Feb. 25, 1980)(Exhibit 10);

10. U.S. Patent No. 4,411,994 for Gilbert, W. et al., "Protein synthesis" issued Oct. 25, 1983 (filed Jun. 8, 1978) (Exhibit 11);

11. U.S. Patent No. 4,634,665 for Axel, R. et al., "Processes for inserting DNA into eucaryotic cells and for producing proteinaceous materials" issued Jan. 6, 1987 (filed Aug. 11, 1983)(Exhibit 12);

12. U.S. Patent No. 5,179,017 for Axel, R. et al., "Processes for inserting DNA into eucaryotic cells and for producing proteinaceous materials" issued Jan. 12, 1993 (filed Jun. 18, 1991)(Exhibit 13)

13. U.K. Patent No. 1,521,032 for Pioli, D. et al., "Biological treatment," published Aug. 9, 1978 (Exhibit 14);

14. U.K. Patent Application No. 2,007,675 for Itakura, K., "Synthetic DNA and process therefor," published May 23, 1979 (Exhibit 15);

15. U.K. Patent Application No. 2,007,676 for Itakura, K. and Riggs, A.D., "Method for microbial polypeptide expression," published May 23, 1979 (Exhibit 16);

16. U.K. Patent Application No. 2,008,123 for Riggs, A.D., "Method for microbial polypeptide expression," published May 31, 1979 (Exhibit 17);

17. U.K. Patent Application No. 2,010,847 for Wacker, A., "A process for the production of insulin-producing cells," published July 4, 1979 (Exhibit 18);

18. European Patent Publication No. 0022685 for Garapin, F. and Garapin, C-A, "Vecteurs pour le transfert et l'expression de materiel genetique et procede pour leur detection" Institut Pasteur, published Jan. 21, 1981 (Exhibit 19);

19. European Patent Publication No. 0037723 for Bell, G. et al. "Expression of hormone genomic clones" The Regents of the University of California, published Oct. 14, 1981 (Exhibit 20);

20. European Patent Publication No. 0038765 for Tiollais, P. et al., "Procede de transformation de cellules, notamment eucaryotes, par un ADN originaire des virus de l'hepatite, plus particulierement du virus de l'hepatite viral B, et preparation contenant les produits d'expression desdits ADN" Institut National de la Sante et de la Recherche Medicale, published Oct. 28, 1981 (Exhibit 21);

21. Alt, F.W. et al. (1978) "Selective multiplication of dihydrofolate reductase genes in methotrexate-resistant variant of cultured murine cells." The Journal of Biological Chemistry, 253:1357-1370 (Exhibit 22);

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amethopterin-resistant Chinese hamster cells in vitro." Cancer Research, 32:153-161 (Exhibit 26);

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35. Chang, A., et al. (1978) "Phenotypic expression in E. coli of a DNA sequence coding for mouse dihydrofolate reductase." Nature, 275:617-624 (Exhibit 34);

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evolutionary divergence of two homologous pairs of introns." Nature 276:37-44 (Exhibit 81);

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102. Wigler, M. et al. (1979b) "DNA-mediated transfer of the adenine phosphoribosyltransferase locus into mammalian cells." PNAS, 76:1373-1376;

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113. Zakai, N. et al. (1977) "Membrane ultrastructural changes during calcium phosphate-induced fusion of human erythrocyte ghosts." Proc. Natl. Acad. Sci., 74:2417-2421 (Exhibit 91).

Applicants would like to point out to the Examiner that the subject application, U.S. Serial No. 08/484,136, filed June 7, 1995, is a continuation of U.S. Serial No. 08/395,520, filed February 27, 1995, which is a continuation of U.S. Serial No. 08/217,007, filed March 23, 1994, which is a continuation of U.S. Serial No. 07/866,800, filed June 26, 1992, which is a continuation of U.S. Serial No. 07/716,915, filed June 18, 1991, now U.S. Patent No. 5,179,017, issued January 12, 1993, which is a divisional of U.S. Serial No. 07/346,089, filed May 2, 1989, which is a continuation of U.S. Serial No. 06/915,273, filed October 3, 1986, which is a divisional of U.S. Serial No. 06/522,408, filed August 11, 1983, now U.S. Patent No. 4,634,665, issued January 6, 1987, which is a divisional of U.S. Serial No. 06/124,513, filed February 25, 1980, now U.S. Patent No. 4,399,216, issued August 16, 1983.

Applicants submit herewith as Exhibit 92 a June 10, 1981 PCT Search Report issued for International Application No. PCT/US81/00240 which claims the priority of U.S. Serial No. 06/124,513, filed February 25, 1980, now U.S. Patent No. 4,399,216, issued August 16, 1983, from which the subject application claims priority. Applicants point out that references 1, 17, 54, 55, 60, 66, 67, 99, 102-104, and 111 were cited in the June 10, 1981 PCT Search Report.

Applicants submit herewith as Exhibit 93 a January 14, 1983 EPO Partial Search Report issued for European Application No. 81 90 0787 which claims the priority of U.S. Serial No. 06/124,513, filed February 25, 1980, now U.S. Patent No. 4,399,216, issued August 16, 1983, from which the subject application claims priority. Applicants point out that references 18-20, 35, and 105 were cited in the January 14, 1983 EPO Partial Search Report.

Applicants submit herewith as Exhibit 94 a June 20, 1983 EPO Supplementary Search Report for European Application No. 81 90 0787 which claims the priority of U.S. Serial No. 06/124,513, filed February 25, 1980, now U.S. Patent No. 4,399,216, issued August 16, 1983, from which the subject application claims prioirty. Applicants point out that references 18-20, 35, 44, and 105 were cited in the June 20, 1983 EPO Supplementary Search Report.

Applicants draw the Examiner's attention to the fact that references 21, 55, 60, 70, 72, 75, 83, 90, 96, 99, 102-104, and 108 were cited in an opposition to the grant of European Patent No. 0 045 809 issued to The Trustees of Columbia University In The City of New York which claims the priority of International Application No. PCT/US81/00240 which claims priority from U.S. Serial No. 06/124,513, filed February 25, 1980, now U.S. Patent No. 4,399,216, issued August 16, 1983, from which the subject application claims priority.

Applicants draw the Examiner's attention to the fact that references 30, 35, 45, 49, 52, 53, 55, 60, 71, 72, 75, 79, 80, 83, 95, 100, 101, and 102-104 were cited in oppositions to Japanese Application No. 501133/81, filed February 23, 1981, which claims priority from International Application No. PCT/US81/00240 which claims priority from U.S. Serial No. 06/124,513, filed February 25, 1980, now U.S. Patent No. 4,399,216, issued August 16, 1983, from which the subject application claims priority.

In accordance with 37 C.F.R. § 1.98(a)(3), applicants submit a concise description of references 18, 20, 30, 53, 71, 79, and 80 which are not in English.

European Patent Publication No. 0022685 for Garapin, F. et al., "Vecteurs pour le transfert et l'expression de materiel genetique et procede pour leur detection" Institut Pasteur, published Jan. 21, 1981, reference 18 above, attached hereto as Exhibit 19, which is in French, discloses the use of vectors for the transfer and expression of genetic material and processes for detecting said transfer.

European Patent Publication No. 0038765 for Tiollais, P. et al., "Procede de transformation de cellules, notamment eucaryotes, par un ADN originaire des virus de l'hepatite, plus particulierement du virus de l'hepatite viral B, et preparation contenant les produits d'expression desdits ADN" Institut National de la Sante et de la Recherche Medicale, published Oct. 28, 1981, reference 20 above, attached hereto as Exhibit 21, which is in French, discloses a process for cellular transformation, particularly eukaryotes, with hepatitis virus DNA, especially hepatitis virus B, and a preparation containing the product expressed by said DNA.

Biochemistry Dictionary, 2nd Ed. (1990) Tokyo Kagaku Dojin pp. 69 and 1343, reference 30 above, attached hereto as Exhibit 29, which is in Japanese, discloses that methotrexate is methylaminopterin and aminopterin has a similar chemical structure to methotrexate.

Kodansha Scientific (1983) Cell Culture Manual, pp. 194-195, reference 53 above, attached hereto as Exhibit 50, which is in Japanese, discloses that mouse L cells are fibroblasts.

Nikkei Biotechnology (1991) The Latest Technical Term Dictionary, pp. 515 and 565, reference 71 above, attached hereto as Exhibit 61, discloses that HAT medium includes hypoxanthine, aminopterin, and thymidine and is used to test cultured cells for transformation and a typical plasmid used for recombinant DNA testing is pBR322 of E. coli.

Protein, Nucleic Acid, Enzyme 20(6):574-580 (1975), reference 79 above, attached hereto as Exhibit 66, which is in Japanese, discloses recombination selective method and the uses of drug resistance as markers of selective method.

Protein, Nucleic Acid Enzyme 22(5):354-356 (1977), reference 80 above, attached hereto as Exhibit 67, which is in Japanese, discloses that the selection of a transformant is performed by a marker carried on a vector, for example, the tetracycline resistance of the pSC101 vector or the colicin resistance of Col E1 factor, where plaque formation indicates transformation.

Applicants have previously filed an Information Disclosure Statement with copies of the references numbered above as 24, 26, 49, 54, 55, 60, 62, 65, 67, 68, 72, 75, 76, 94, 96, 99, 100, 102-104, 107, 108, 110, and 111 in connection with U.S. Serial No.08/395,520, filed February 27, 1995 from which the subject application claims priority. Accordingly, copies of references

numbered above as 24, 26, 49, 54, 55, 60, 62, 65, 67, 68, 72, 75, 76, 94, 96, 99, 100, 102-104, 107, 108, 110, and 111 are not required to be provided pursuant to 37 C.F.R. §1.98(d). Applicants will, however, gladly supply the Examiner with copies of said references upon request.

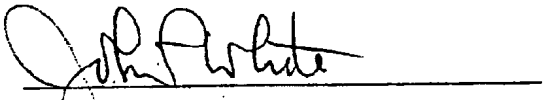
In accordance with 37 C.F.R § 1.17(p), applicants herewith submit a check in the amount of two hundred forty dollars ($240.00) payable to the United States Patent and Trademark Office as the fee for an information disclosure statment.

No fee, other than the two hundred forty dollar ($240.00) fee for an information disclosure statement, is deemed necessary in connection with the filing of this information disclosure statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned

attorney invites the Examiner to telephone him at the number provided below.

Respectfully submitted,



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